Urinary zinc stable isotope signature as indicator for cancer types with disrupted zinc metabolism

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Zinc (Zn) is an essential biometal which determines the catalytic and structural role of proteins. Its abundance is generally tightly regulated in the human body. Cancer development and progression dysregulates the Zn abundance in the body. Pancreatic, breast and prostate cancers are all known to alter the Zn metabolism. Diagnostic and prognostic tools for early detection of pancreatic cancer and more reliable diagnosis of prostate cancer are urgently needed. Urinary Zn concentrations and Zn stable isotope signature ($\delta^{66/64}$Zn) may be a non-invasive approach in tracing malignancy-induced changes in Zn metabolism.

Our results show that statistically significant Zn concentration and isotopic changes ($p = 0.002$) are present in the urine of pancreatic cancer patients (n = 17) that are not seen in healthy controls (n = 33). The preferential excretion of isotopically light Zn in pancreatic cancer likely reflects the dysregulation of metalloproteins. Urine samples from prostate cancer patients (n = 21) have been assessed to see if a disease related Zn isotopic shift in urine occurs, and if so, whether the Zn isotopic signature differs from that exhibited in pancreatic cancer patients. The analysis showed that the isotopic shift in Zn metabolism is not reflected in the urine as there is no systematic difference between the prostate cancer group and the male healthy controls (n = 8; $p = 0.11$). This can be explained by the vastly segregated prostate Zn cycle from other body fluids such as urine.

Thus, urinary Zn isotopes show promise as a novel, non-invasive approach for pancreatic cancer detection that can also help potentially detect Zn dysregulation compared to a healthy population and other types of cancer with an altered Zn metabolism (*e.g.*, prostate cancer).